REMARKS

Claims 4-9, 19, 29 and 30 have been amended by including the modifier "isolated."

Claims 5 and 8 have been amended by deleting the phrase "or homologues thereof."

Claims 16 and 19 have been amended by further limiting the claims.

No new matter has been added.

1. CLAIM OBJECTIONS

The Examiner has objected to claims 5, 8, 16 and 19 as failing to further limit the subject matter of a previous claim.

Applicants have amended the claims, thereby overcoming the objections.

The Examiner has also objected to claims 6 and 19 for misspelling the word "monospecific" and "HopC."

Applicants have corrected the misspelling, thereby overcoming the objections.

The Examiner has objected to claims 4-5, 7-8 and 29-30 for failure to recite "The isolated..."

Applicants have amended the claims, thereby overcoming the objections.

2. REJECTIONS UNDER 35 USC §112, FIRST PARAGRAPH

The Examiner has rejected claims 3-5, 6-8, 16, 19 and 27-30 for lack of written description. The Examiner states that the written description in the application sets forth nucleic acid and amino acid sequences for BabA and BabB (SEQ ID NOs: 1-8). She contends that there is no support for sequences that are homologous to SEQ ID NOs: 1-8.

While not agreeing with the Examiner's conclusion, but in an effort to move the application forward, Applicants have amended the claims by deleting the phrase "or homologs thereof," thereby overcoming the rejection.

3. REJECTIONS UNDER 35 USC §112, SECOND PARAGRAPH

The Examiner has rejected claims 5 and 8 as indefinite for recitation of the phrase "or homologs thereof."

While not agreeing with the Examiner's conclusion, but in an effort to move the application forward, Applicants have amended the claims by deleting the phrase "or homologs thereof," thereby overcoming the rejection.

4. DOUBLE-PATENTING

The Examiner states that should claims 27 and 29; and claims 28 and 30 be found allowable, claims 29 and 30 will be objected to as being a substantial duplicate of claims 27 and 28. Applicants respectfully traverse.

Claims 27 and 28 depend on claim 4, which is directed to an immunoglobulin composition. On the other hand, Claims 29 and 30 depend from claim 6, which is an isolated antibody. Claims 27 and 28 provide a range of molecular weights, where claims 28 and 30 provide only a single value for molecular weight. An isolated antibody is distinct from an immunoglobulin composition and a single molecular weight value is distinct from a range of molecular weights. In neither case do the claims "cover the same thing, despite a slight difference in wording" as stated by the Examiner. Consequently, Applicants request reconsideration and removal of the rejection.

5. Claim rejections under 35 USC §102

5.1 Novelty rejections based on Durrant et al., 1993

The Examiner states "Durrant et al. disclose a rat polyclonal antiserum that comprises purified immunoglobulin anti-idiotypic antibodies that evidence the Lewis B antigen epitope confirmation, which would specifically bind to and form a complex with *Helicobacter pylori* Lewis B antigen binding antigen as Durrant showed that the rat antiserum comprised anti-ID Lewis B antigen presenting immunoglobulins."

The Examiner points to Essery et al to show that an anti-idiotypic antibody which evidences the Lewis B antigen structure disclosed in Durrant would bind to the BabA protein which binds to Lewis B antigen. Essery discloses that 1 of 3 strains of Helicobacter pylori bound to the anti-id Lewis A IgG monospecific antibody. Applicants respectfully traverse.

The antibodies against Lewis A and Lewis B recognize unique antigens and the specificity is due to sequence differences in the hypervariable region. Thus, by definition, the anti-idiotypic antisera raised by Essery et al are not directed against the antigen binding site, but rather a paratope which is shared to some, albeit modest, degree that binds the tested monoclonals (anti- Lewis A and anti- Lewis B). The reference claims that this paratope is not shared with 4 other monoclonal antibodies, but no data is provided to support this claim (see Essery et al., page 19 "Specificity of the proteins A sepharose reagent"). In fact, Essery et al states "the paratope of the Fab portion of the anti-idiotypic antibody appears to have a structure <u>similar</u> to the Lewis A antigen" (emphasis added), it does <u>not</u> say identical to the Lewis A antigen.

If one argues that there is indeed specific binding to the anti-idiotypic antiserum to BabA, it follow that this antigen is also present on other bacteria, such as *N. gonorrhoeae*, and fungi such as *C. ablicans*. Here, 1 of 2 *N. gonorrhoeae* strains reacted (see page 19, column 2, last paragraph, lines 5-7) and 1 of 2 *C. ablicans* strains reacted (see page 20, column 1, first paragraph, lines 5-8). But these microorganisms do not express BabA, therefore the anti-idiotypic antiserum described by Essery et al must recognize **another** protein or structure.

Applicants also note that the claims have been amended to require that the BabA protein binds both Lewis B and H-1 blood group antigen-glycoconjugates. This is missing from Durrant.

In view of the above, Applicants respectfully request reconsideration and removal of the rejection.

5.2 NOVELTY REJECTIONS BASED ON UEMURA ET AL (U.S. 5,258,177)

The Examiner has rejected claims 3-8, 16, 19 and 27-30 as being anticipated by Uemura et al in light of evidence provided by Boren et al. The Examiner contends that the monospecific immunoglobulin compositions of Uemura et al that comprise secretory sIgA from human colostrum specifically bind BabA because the claims do not specifically recite that the claimed antibodies bind to BabA via the antibody hypervariable region. Applicants respectfully traverse.

Those of skill in the art understand that specific binding is carried out by the antigen binding site of the specific antibody, as determined by the sequence of the hypervariable region. If binding to a sugar moiety on some antibodies would confer specific binding, there would be no need for immunization in order to raise anti-BabA-specific antibodies. Applicants note

that since skilled artisans believe antibodies to act through the hypervariable region, this is understood and is no longer stated in discussions or presentations of antibodies. Thus, Applicants respectfully request reconsideration and removal of the rejection.

6. CLAIM REJECTIONS UNDER 35 USC §103

The Examiner has rejected claim 2 as obvious over Boren (1995) in view of Foster et al. (U.S. Pat. No. 4,444,879). The Examiner contends that Boren teaches detection of the presence of a Helicobacter pylori blood group binding protein antigen using binding of colostum sIgA in a method of detecting the presence of absence of the blood group antigen in a sample. The Examiner acknowledges that Boren fails to show the incorporation of the IgA immunoglobulin/antibody into kit form.

The Examiner contends that Foster et al. discloses formulation of immunoglobulin/antibody compositions into kit form. Based on these disclosures, the Examiner contends that it would have been obvious for a person skilled in the art to modify the Boren composition and form a kit as taught by Foster to obtain the present invention. The Examiner's reasons for why the skilled artisan would be motivated to do so are lengthy (see page 13 of the Office Action) and are not repeated here. Applicants respectfully traverse.

It would appear that the Examiner is using impermissible hindsight in order to frame the rejection, which is improper. The Boren et al. publication reports experiments identifying the receptor on the surface of gastric mucosal cells to which *H. pylori* proteins bind in the process of attaching to gastric mucosal cells. Specifically, Boren et al. reports that pre-incubation of *H. pylori*

with secretory IgA isolated from human colostrum inhibited subsequent binding by *H. pylori* to gastric mucosal cells. In contrast, the same pre-incubation experiment conducted with IgA antibodies isolated from serum failed to inhibit *H. pylori* binding to gastric mucosal cells (see pg 32). The conclusion drawn from this experiment is that the colostrum secretory IgA antibodies present the same attachment-mediating receptor to *H. pylori* that the gastric mucosal cells do.

The distinction between secretory IgA antibodies isolated from colustrum and IgA antibodies isolated from serum is that the colostrum secretory IgA antibodies are conjugated with carbohydrate whereas serum IgAs are not. Based on this distinction, Boren et al. ran experiments with monoclonal antibodies directed against carbohydrate antigens, specifically the Lewis A and Lewis B antigens. Only secretory IgA isolated from colostrum detected Lewis A and Lewis B antigens: the Lewis antigens were not detected by IgA antibodies from sera. The conclusion that Boren et al. draws from this result is that Lewis A and Lewis B carbohydrates are candidates for the receptor to which *H. pylori* binds to attach to gastric mucosal cells (see Boren et al. (1993) Science 262:1892-1895; attached).

Through additional experiments, Boren et al. identifies Lewis B protein conjugates as potent inhibitors of *H. pylori* attachment to gastric mucosal cells, whereas Lewis A protein conjugates do not have such inhibitory activity. The conclusion drawn here is that "Lewis B antigen is an essential part of the cell surface H. pylori receptor" (see Boren and Falk, 1995, page 32). At no point does Boren et al. describe any antisera or antibody that binds to the adhesin protein via its hypervariable region. That is, the secretory IgA molecules do not specifically bind adhesin, rather

adhesin specifically binds the fucosylated Lewis B antigen presented on the secretory IgA molecule.

The instant application describes **monospecific** antisera and antibodies raised against BabA protein from *Helicobacter pylori* that specifically recognize and bind to BabA protein through their hypervariable region. Stated clearly, the Boren et al. antibodies bind to a carbohydrate antigen, the Lewis B carbohydrate, whereas the antisera and antibodies of the present invention bind to protein antigen, the adhesin protein of *H. pylori*. Thus, there would not be any motivation for the skilled artisan to modify the Boren composition.

The Foster et al. reference does not fill the void present in the Boren et al. reference simply because Foster teaches kits containing immunoglobulin/antibody compositions.

In view of the above, Applicants respectfully request reconsideration and removal of the rejections.

Applicants submit that the present amendment places all of the claims remaining in the case, including newly added claims, as defining non-obvious, patentable subject matter. Reconsideration of the rejections and allowance of the claims are respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is requested to contact Susan W. Gorman (Reg. No. 47,640) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursant to the provisions of 37 C.F.R §§ 1.17 and 1.136(a), Applicants petition for an extension of one (1) month to July 6, 2006 for the period in which to file a response to the Office Action dated March 6, 2006. The Commissioner is authorized to charge Deposit Account No. 02-2448 in the amount of $60.00 for this extension of time fee.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

LRS/SWG/sbp
0825-0176P

By _____

Leonard R. Svensson, #30,330
P.O. Box 747
Falls Church, VA 22040-0747
(714) 708-8555

Attachments: